Shot to the Heart: CV Risk Reduction Through Vaccination

Welcome and Introductions

Shelley Zieroth

MD, FCCS, FHFSA (hon), FESC, FACC, FHFA, FRCPC

Accreditation

This event is an Accredited Group Learning Activity (Section 1) as defined by the Maintenance of Certification Program of the Royal College of Physicians and Surgeons of Canada, and approved by the Canadian Cardiovascular Society. You may claim a maximum of 0.5 hour (credits are automatically calculated).

Faculty

Chair:

- Shelley Zieroth, MD, FCCS, FHFSA (hon), FESC, FACC, FHFA, FRCPC

Presenter:

- Jacob Udell, MD, MPH, FRCPC

Disclosures

	Dr. Shelley Zieroth
Any direct financial payments including receipt of honoraria	No disclosures
Membership on advisory boards or speakers' bureaus	AstraZeneca, Bayer, BMS, Boehringer Ingelheim, Cytokinetics, Eli Lilly, GSK, Janssen, Medtronic, Merck, Novartis, Novo-Nordisk, Otsuka, Pfizer, Roche, Salubrisbio, Servier and Vifor Pharma.
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This program has received an educational grant from GSK Canada. This program was developed by the Canadian Heart Failure Society and was planned to achieve scientific integrity, objectivity and balance.

Symposium Agenda

2 mins	Welcome and Introduction Dr. Shelley Zieroth
18 mins	The importance of vaccination with downstream impacts on cardiovascular disease (Addressing the importance of Shingles and RSV vaccines). Dr. Jacob Udell
8 mins	Q&A Period Dr. Shelley Zieroth and Dr. Jacob Udell
2 mins	Conclusion Dr. Shelley Zieroth

Housekeeping

- To collect your MOC Section 1 credits, please remember to complete both the session evaluation and the congress evaluation
- The evaluation QR code can be found on your tables and will be displayed on the screen after the presentation

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Shot to the Heart: CV Risk Reduction Through Vaccination

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Disclosures

	Dr. Jacob Udell
Any direct financial payments including receipt of honoraria	Amgen, AstraZeneca, Boehringer Ingelheim, Eli Lilly, GSK, Sanofi
Membership on advisory boards or speakers' bureaus	Amgen, Boehringer Ingelheim, Janssen, Merck, Novartis, Novo Nordisk, Sanofi
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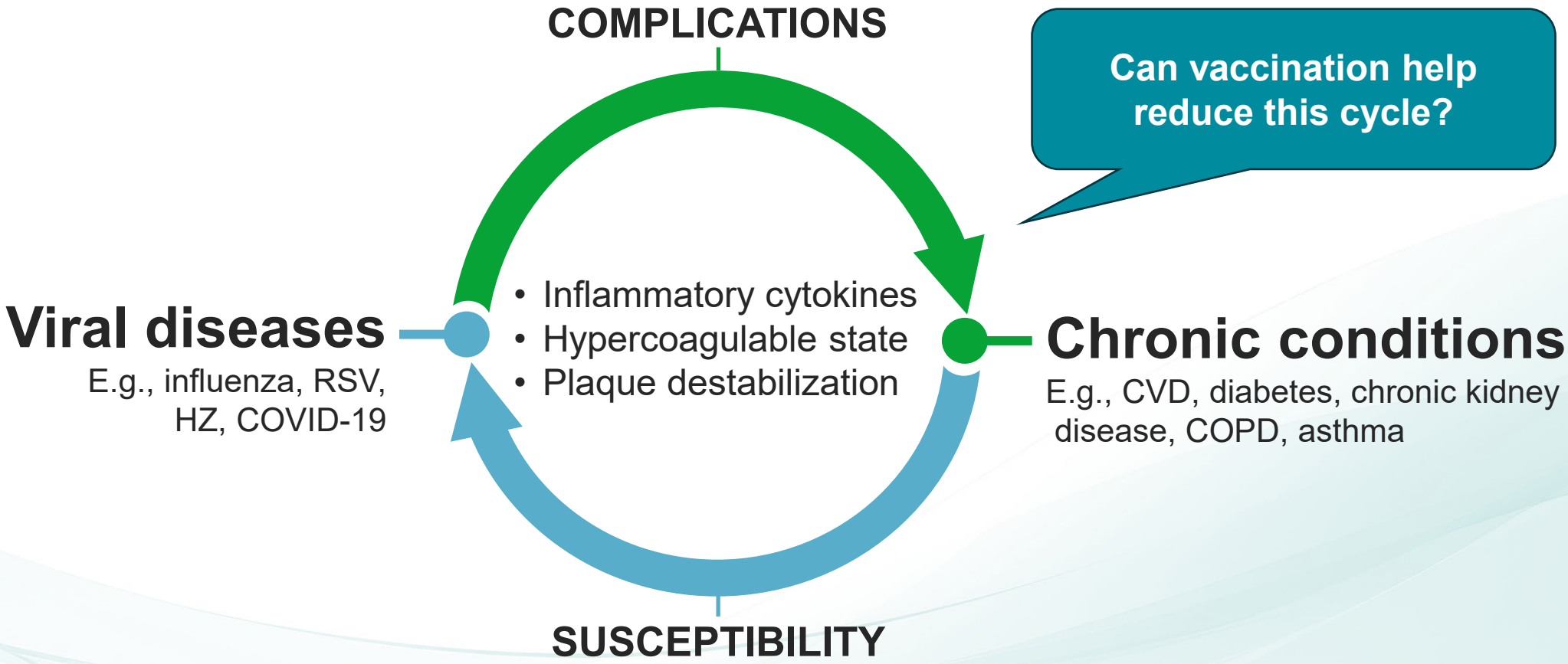
Learning Objectives

By the end of this session, participants will be able to:

1. Explain how changes in immune function that coincide with aging and cardiovascular conditions, including HF, are associated with increased susceptibility to viral infections like influenza, herpes zoster (shingles), and respiratory syncytial virus (RSV)
2. Highlight key data pointing to the association between viral infections on downstream CV complications in patients with HF
3. Underscore the importance of vaccination against viral infections as a strategy to reduce the risk of CV complications, discussing practical considerations for incorporation into comprehensive HF care plans

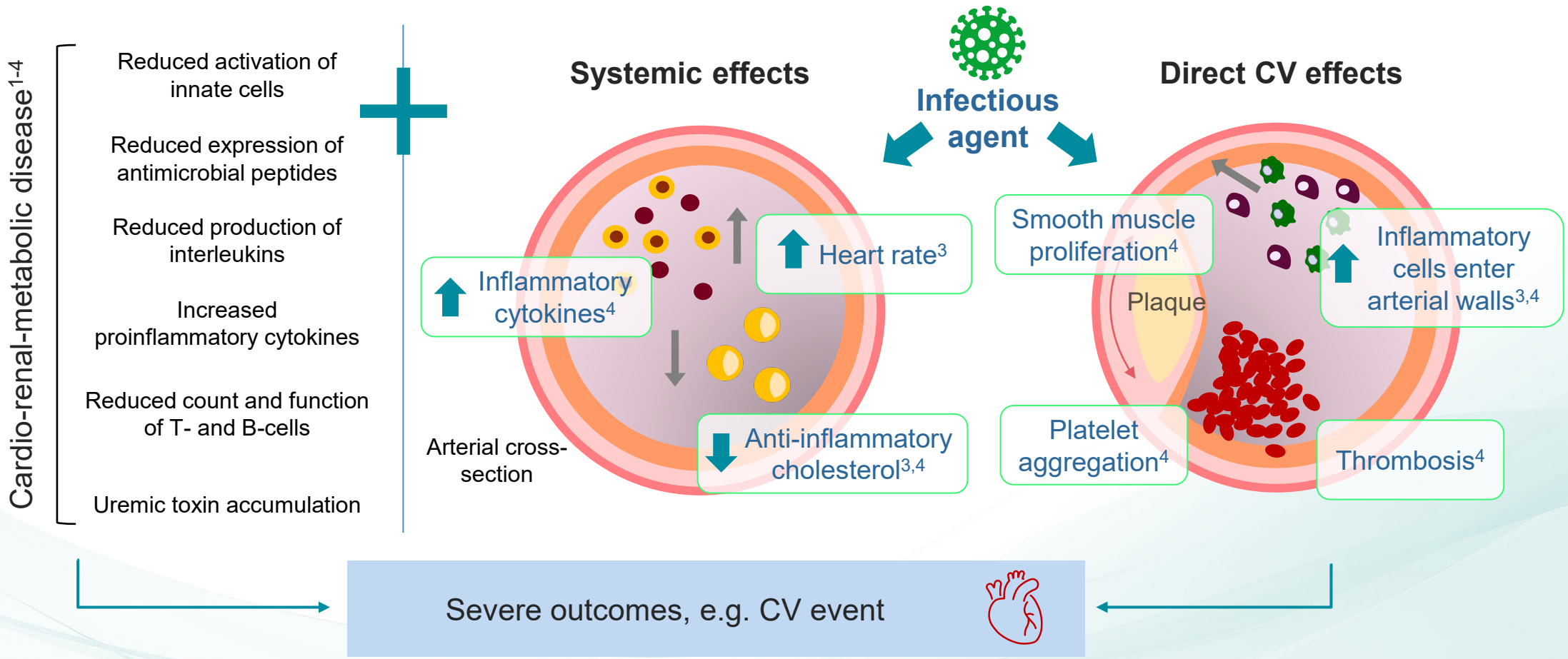
Bidirectional relationship between viral diseases and complications associated with chronic conditions



COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; CVD, cardiovascular disease; HZ, herpes zoster; RSV, respiratory syncytial virus.

1. Quinton LJ, et al. *Physiol Rev*. 2018;98(3):1417-1464. 2. Ivey KS, et al. *Am Coll Cardiol.* 2018;71:1574-83. 3. Toniolo A, et al. *Rev Med Microbiol*. 2019;30:1-17. 4. Nishiga M, et al. Nat Rev Cardiol. 2020;17(9): 543-558. 5. Bhat TA, et al. *Ann Am Thorac Soc.* 2015;12(Suppl 2):S169-S175. 6. Guignard AP, et al. *Infection.* 2014;42:729-735. 7. Marra F, et al. *Open Forum Infect Dis.* 2020;7:ofaa005. 8. Yawn BP, et al. *Vaccines (Basel)*. 2022;10:420. 9. Carey IM, et al. *Diabetes Care.* 2018;41:513-21. 11. Muñoz-Quiles C, et al. *Hum Vaccin Immunother.* 2017;13(11):2606-2611.

Inflammation and immune dysfunction related to underlying disease and acute infection may contribute to severe vascular outcomes



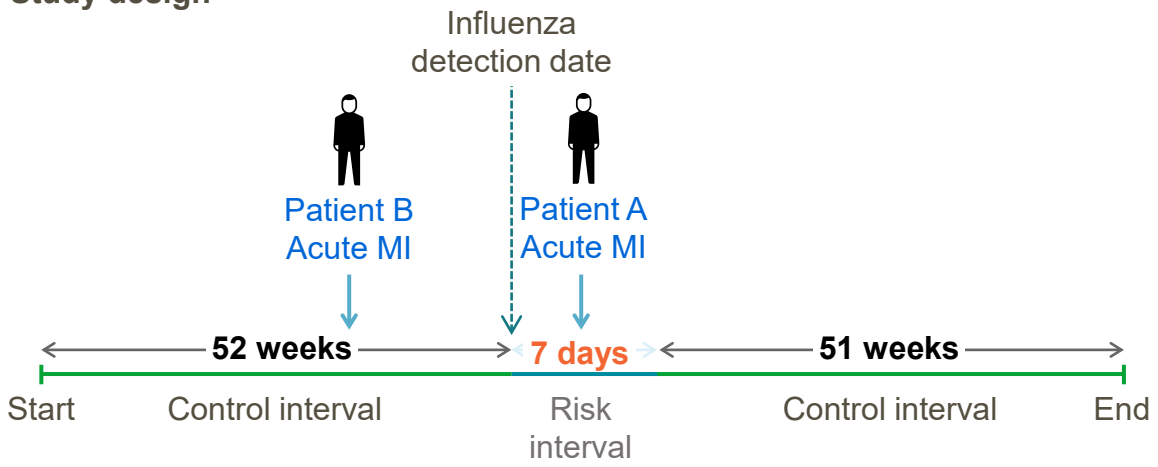
CV, cardiovascular.

1. Toniolo A, et al. *Rev Med Microbiol.* 2019;30:1-17. 2. Ishigami J, Matsushita K. *Clin Exp Nephrol.* 2019;23:437-447. 3. Madjid M, et al. *Tex Heart Inst. J* 2004;31:4-13; 4. Pothineni NV, et al. *Eur Heart J.* 2017;38:3195-201.

Lab-confirmed Influenza, RSV and Other Respiratory Infections Can Trigger an Acute MI[1]

An increase in heart attacks from 3.3/week to 20/week

Study design



N=364 acute MI hospitalisations (332 patients) who had a lab-confirmed influenza diagnosis

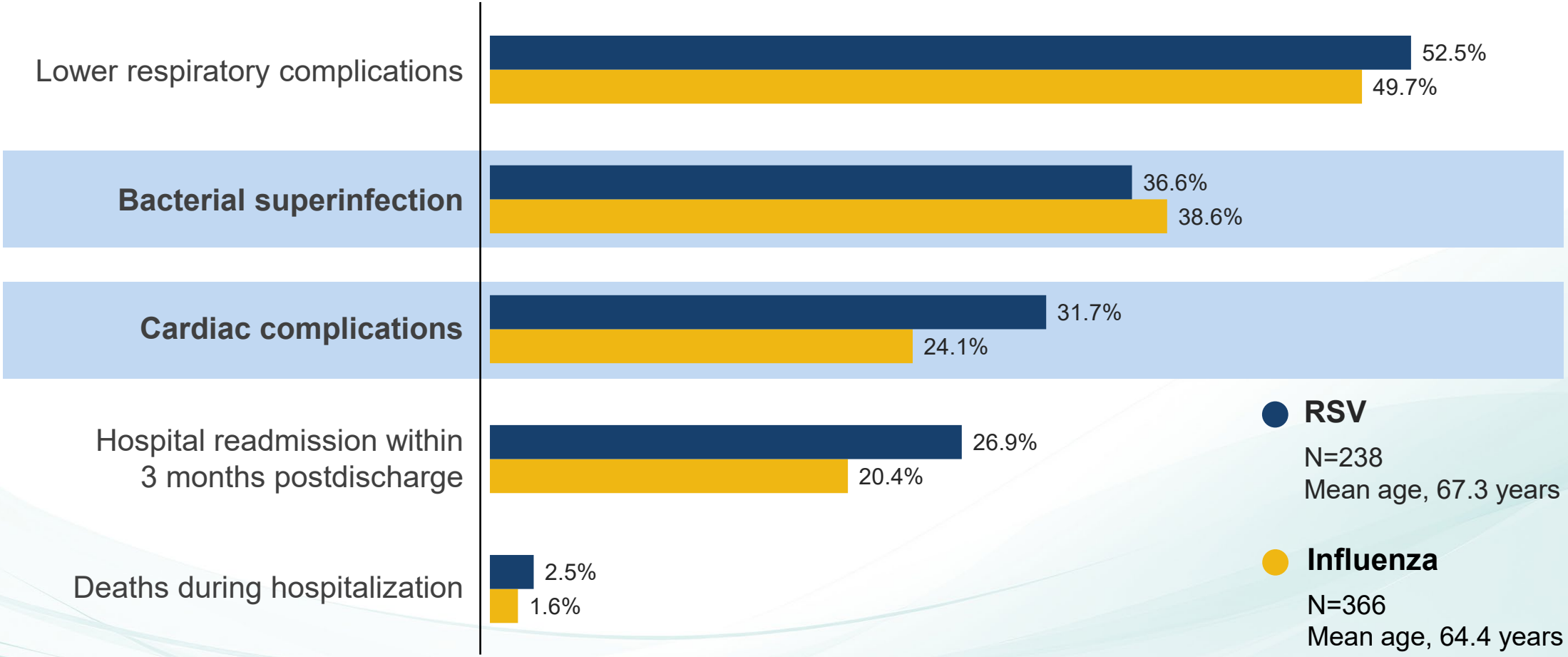
Exposure	Risk ratio (95% CI)
Influenza	
Days 1–7	**6.05 (3.86–9.50)**
Days 8–14	0.60 (0.15–2.41)
Days 15–28	0.75 (0.31–1.81)
Influenza A	**5.17 (3.02–8.84)**
Influenza B	**10.11 (4.37–23.38)**
RSV	**3.51 (1.11–11.12)**
Other resp. viruses	2.77 (1.23–6.24)
Other resp. infection	3.30 (1.90–5.73)

CI, confidence interval; MI, myocardial infarction; RSV, respiratory syncytial virus.

Self-controlled case series study design – patients acted as their own control in periods when they were not exposed vs when they were exposed to influenza and other respiratory viruses in Ontario, Canada.

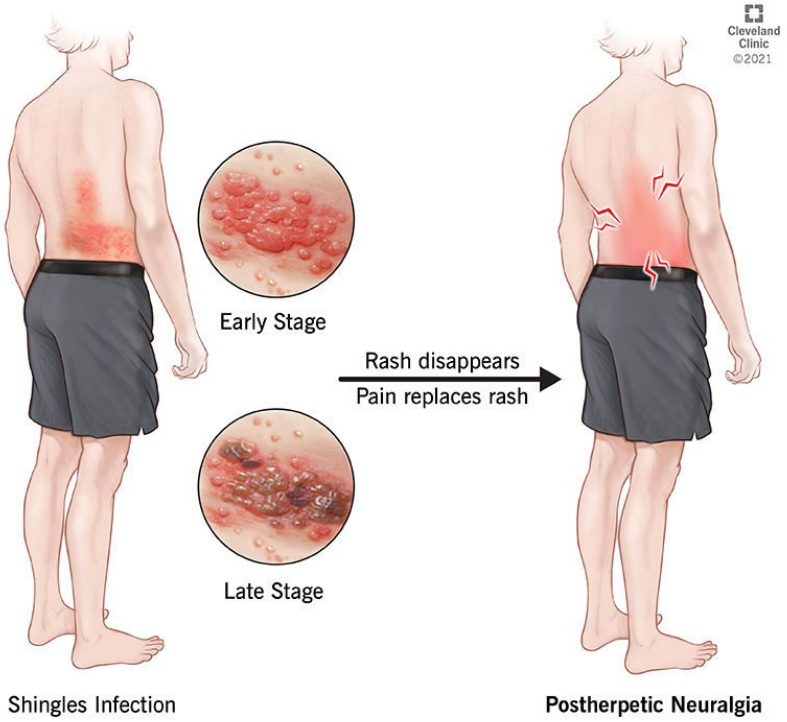
Kwong JC et al. *N Engl J Med* 2018;378:345–353.

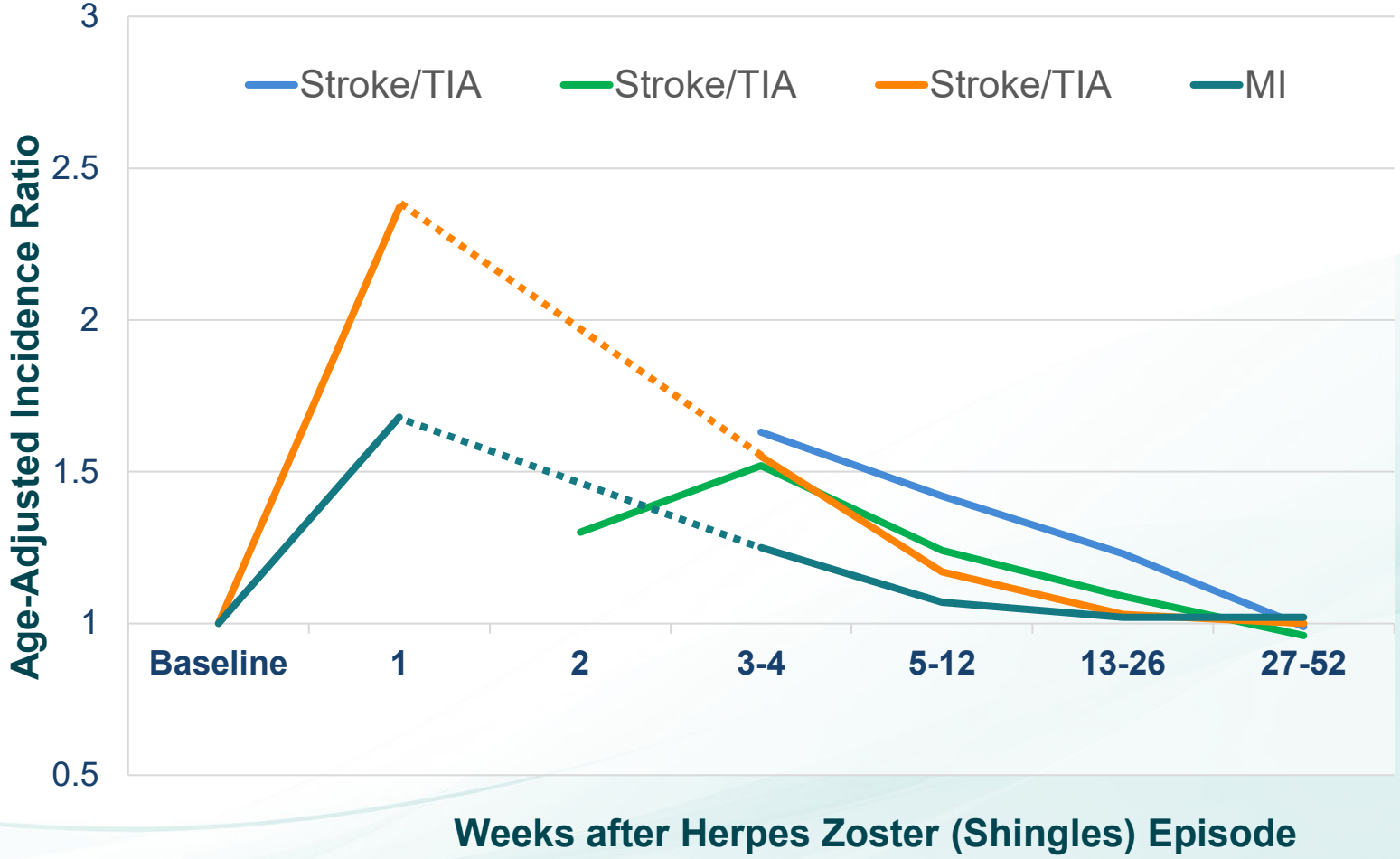
Rates of Complications w/ Respiratory Infection Hospitalizations Similar between RSV and Influenza



Falsey AR, et al. *Open Forum Infect Dis.* 2021;8(11):ofab491.

Herpes Zoster (Shingles) Associated with an Increased Risk of MI/Stroke



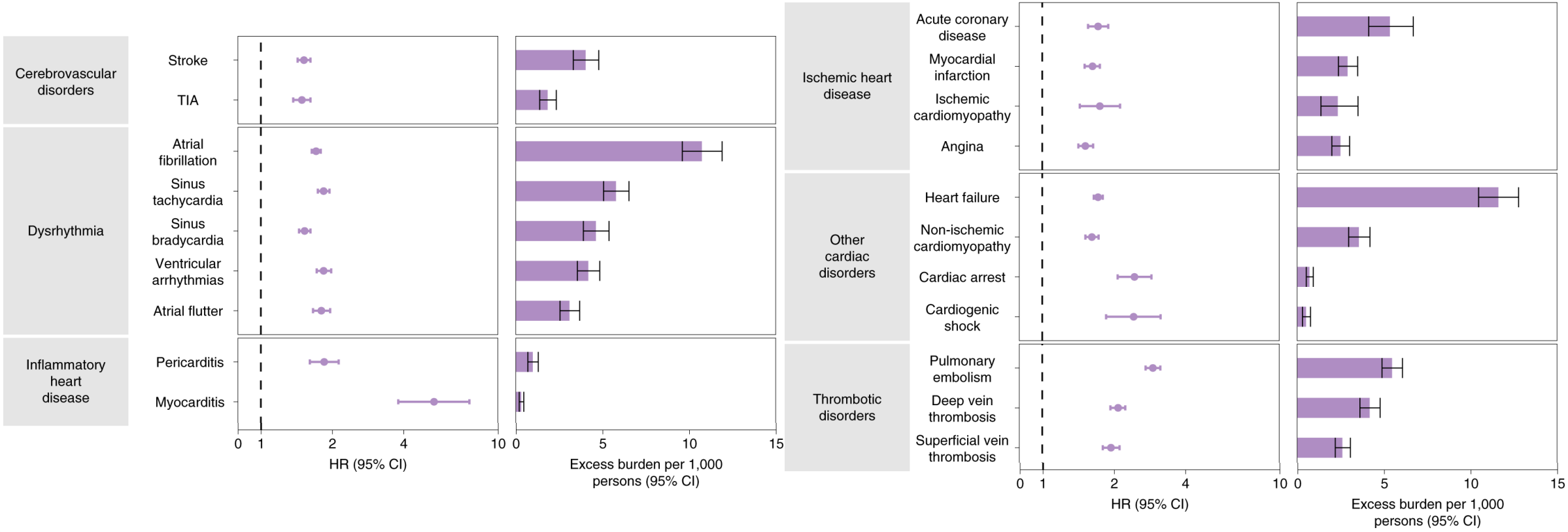


Self-controlled case series study design – patients acted as their own control in periods when they were not exposed vs when they were exposed to herpes zoster (shingles) diagnosis.

Wu PH *et al. J Clin Med* 2019;8(547):1-15. doi:10.3390/jcm8040547.
Langan SM, et al. *Clin Infect Dis* 2014;58:1497-1503. Schink T, et al. *PLoS ONE* 2016;11:e0166554. Minassian C, et al. *PLoS Med* 2015;12:e1001919.

COVID-19 Associated w/ Higher Risk of CV Events[1,2]

A US retrospective COVID-19 case-control* database analysis estimated risks and 12-month burdens of incident post-acute COVID-19 cardiovascular outcomes[1]

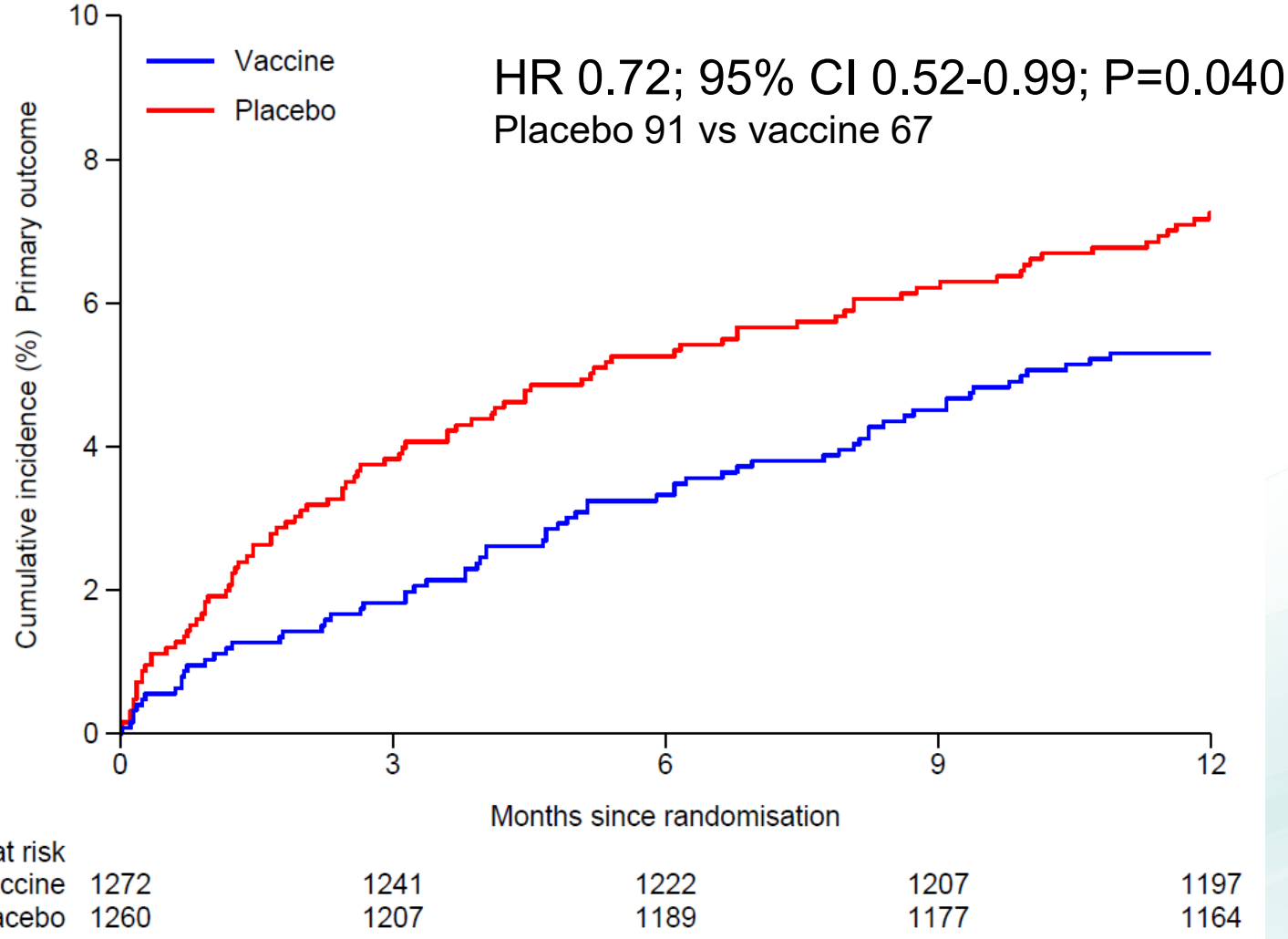


* Using national healthcare databases from the US Department of Veterans Affairs with presented analysis conducted using a cohort of 153,760 individuals with COVID-19, as well as 5,637,647 individuals as contemporary controls. HR = hazard ratio; CI, confidence interval; TIA, transient ischemic attack; US, United States. 1. Xie Y et al. *Nat Med* 2022; 28(1),583–590; 2. Patone M et al. *Nat Med* 2022; 28(1),410-422

IAMI Trial: Reduction in All-cause Mortality, MI, Stent Thrombosis with Influenza Vaccine in Pts w/ Acute CAD

N = 2532

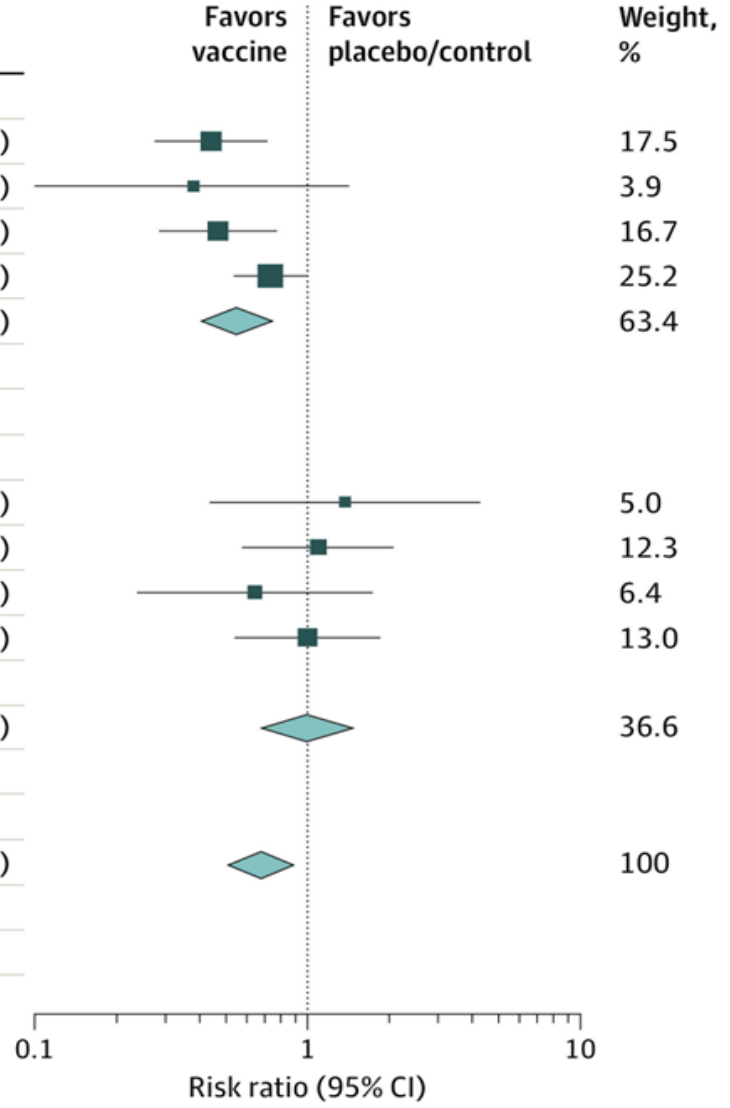
STEMI ~54%
NSTEMI ~45%
Stable CAD <1%



Fröbert O, et al. *Circulation* 2021;144:1476-1484.

Meta-Analysis of Influenza Vaccine RCTs for CV Risk Reduction

Study or subgroup	Vaccine Events	Vaccine Total	Placebo/control Events	Placebo/control Total	Risk ratio, (95% CI)	Weight, %
Recent ACS						
Gurfinkel et al,[19] 2004	18	96	41	97	0.44 (0.28-0.71)	17.5
Ciszewski et al,[20] 2008	3	83	7	74	0.38 (0.10-1.42)	3.9
Phrommintikul et al,[21] 2011	20	221	42	218	0.47 (0.29-0.77)	16.7
Frøbert et al,[7] 2021	67	1266	91	1258	0.73 (0.54-0.99)	25.2
Total events	108	1666	181	1647	0.55 (0.41-0.75)	63.4
Heterogeneity: $\tau^2 = 0.03$; $\chi^2 = 4.50$, df = 3 ($P = .21$); $I^2 = 33\%$						
Test for overall effect: $z = 3.78$ ($P < .001$)						
Stable outpatients						
Govaert et al,[22] 1994	7	927	5	911	1.38 (0.44-4.32)	5.0
Gurfinkel et al,[19] 2004	14	49	13	50	1.10 (0.58-2.09)	12.3
Ciszewski et al,[20] 2008	6	242	10	259	0.64 (0.24-1.74)	6.4
De Villiers et al,[23] 2009	20	1620	20	1622	1.00 (0.54-1.85)	13.0
Frøbert et al,[7] 2021	0	6	0	2	Not estimable	
Total events	47	2844	48	2844	1.00 (0.68-1.47)	36.6
Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 1.14$, df = 3 ($P = .77$); $I^2 = 0\%$						
Test for overall effect: $z = 0.02$ ($P = .98$)						
Total events	155	4510	229	4491	0.68 (0.52-0.90)	100
Heterogeneity: $\tau^2 = 0.05$; $\chi^2 = 11.27$, df = 7 ($P = .13$); $I^2 = 38\%$						
Test for overall effect: $z = 2.73$ ($P = .006$)						
Test for subgroup differences: $\chi^2 = 5.65$; df = 1 ($P = .02$); $I^2 = 82.3\%$						



ACS, acute coronary syndrome; CI, confidence interval; RCT, randomized controlled trial.

Behrouzi B, Bhatt DL, Cannon CP et al… Udell JA. *JAMA Netw Open.* 2022;5:228873.

IVVE: Flu Vaccine in Pts w/ HF

N = 5129

	Influenza vaccine (N=2560)	Placebo (N=2569)	Influenza vaccine vs. Placebo	
	No. of events (%)	No. of events (%)	HR (95% CI)	P value
First primary	380 (14.8)	410 (16.0)	0.93 (0.81-1.07)	0.30
CV death	334 (13.0)	374 (14.6)	0.89 (0.77-1.04)	0.13
All Hosp	388 (15.2)	455 (17.1)	0.84 (0.74-0.97)	0.01
HF Hosp	245 (9.6)	277 (10.8)	0.88 (0.74-1.04)	0.15
Pneumonia	61 (2.4)	104 (4.0)	0.58 (0.42-0.80)	0.0006

Lancet Global Health 2022;10:1835-1844.
CI, confidence interval; CV, cardiovascular; MI, myocardial infarction

Flu Vaccine in HF: Results During vs Outside Influenza Season

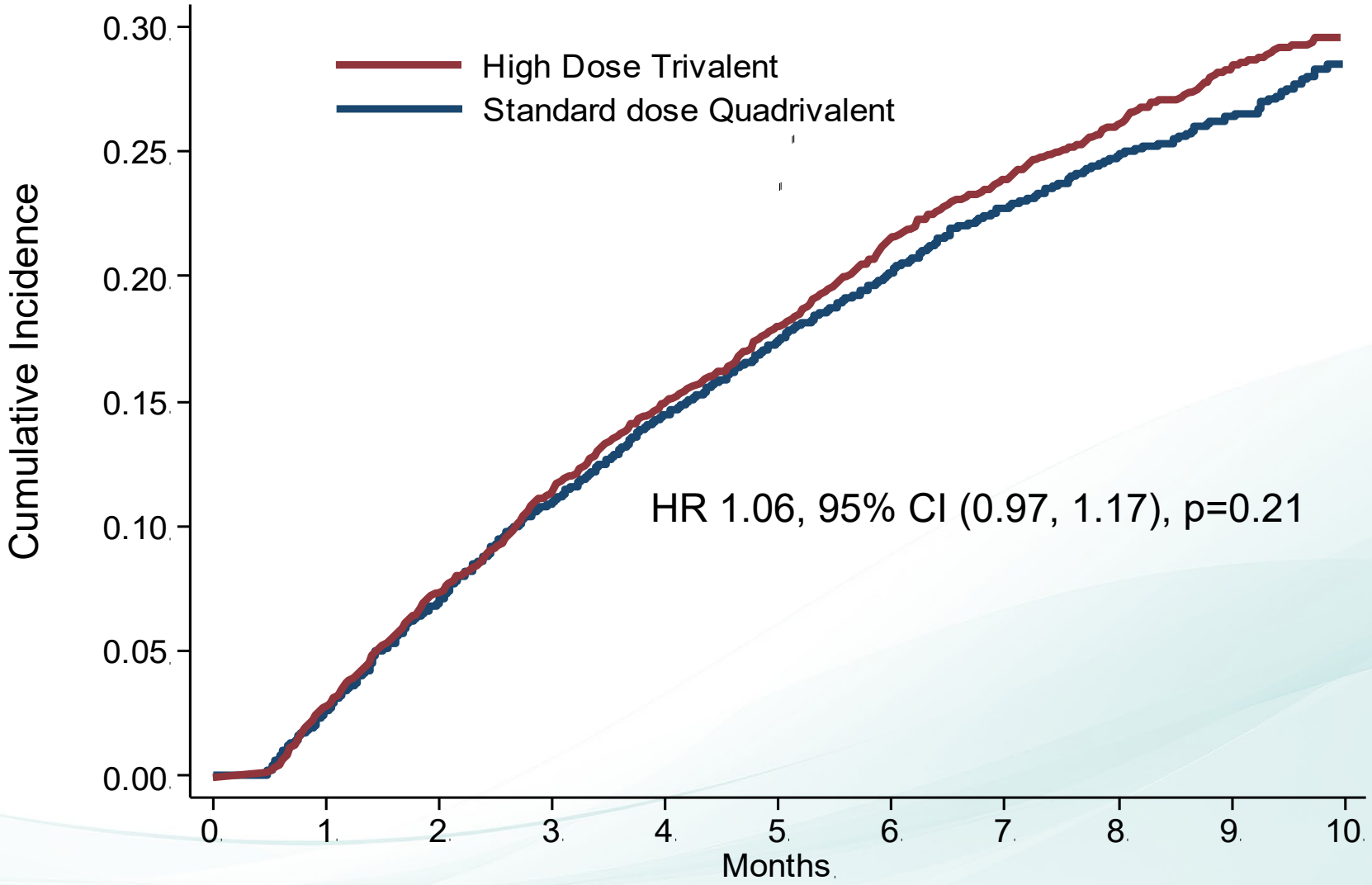
	Peak Influenza			Outside of Peak Season		
	Influenza vaccine	Placebo	Influenza vacc. vs Placebo	Influenza vaccine	Placebo	Influenza vacc. vs Placebo
	No. of events (%)	No. of events (%)	HR (95% CI)	No. of events (%)	No. of events (%)	HR (95% CI)
Primary EP	193.7 (7.7)	227 (9.4)	0.82 (0.68-0.99)	187 (7.5)	173 (6.9)	1.08 (0.88-1.33)
All Hosp	195 (7.8)	230 (9.2)	0.84 (0.69-1.01)	193 (7.9)	225 (9.1)	0.84 (0.70-1.03)
HF Hosp	128 (5.1)	124 (4.9)	1.03 (0.80-1.32)	117 (4.7)	153 (6.1)	0.76 (0.60-0.97)
Pneumonia	28 (1.1)	54 (2.1)	0.51 (0.32-0.81)	33 (1.3)	50 (2.0)	0.65 (0.42-1.01)

Lancet Global Health 2022;10:1835-1844.
HR, hazard ratio.

INVESTED: All-cause Mortality or Cardiopulmonary Hospitalization

N = 5260

HF: 63%
MI: 37%
LVEF <40%: 43%



Vardeny O, Kim K, Udell JA, et al. *JAMA* 2021;325:39-49.

RSV Vaccine Efficacy Against RSV-Lower Respiratory Tract Disease* with ≥1 Comorbidity, though Low Event Rates[1]

Season 1

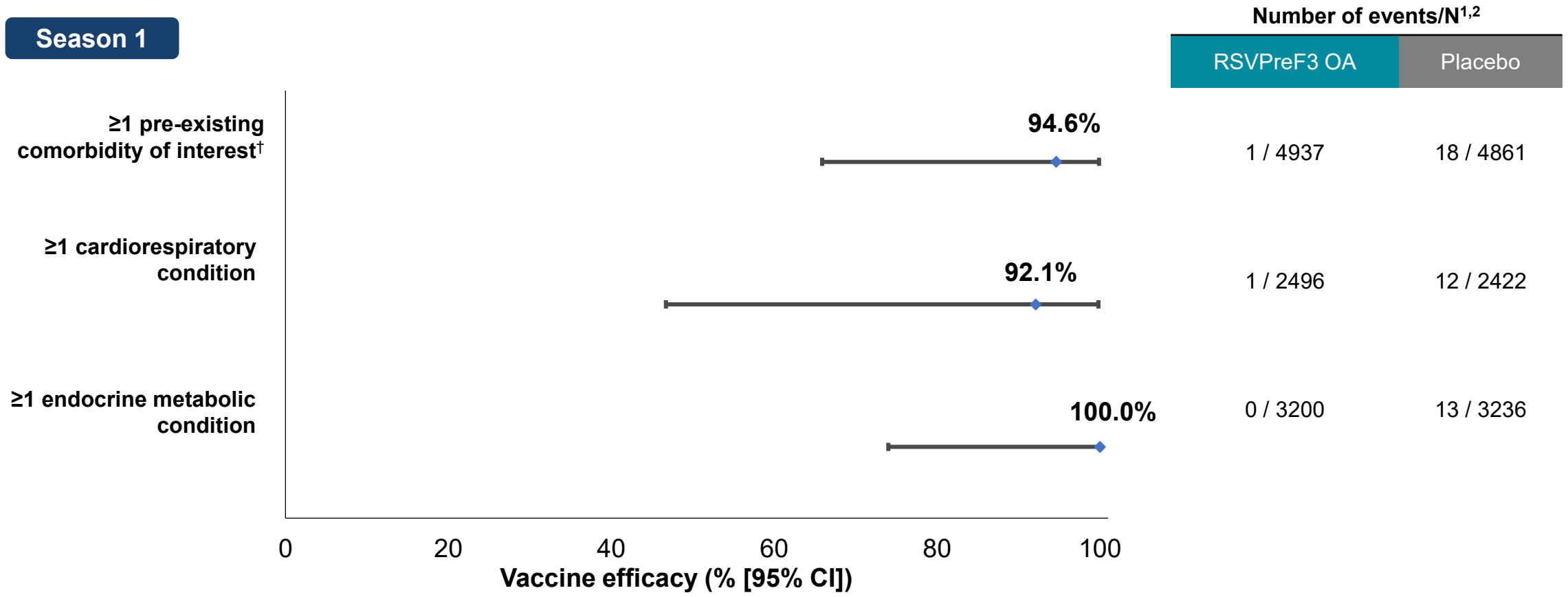
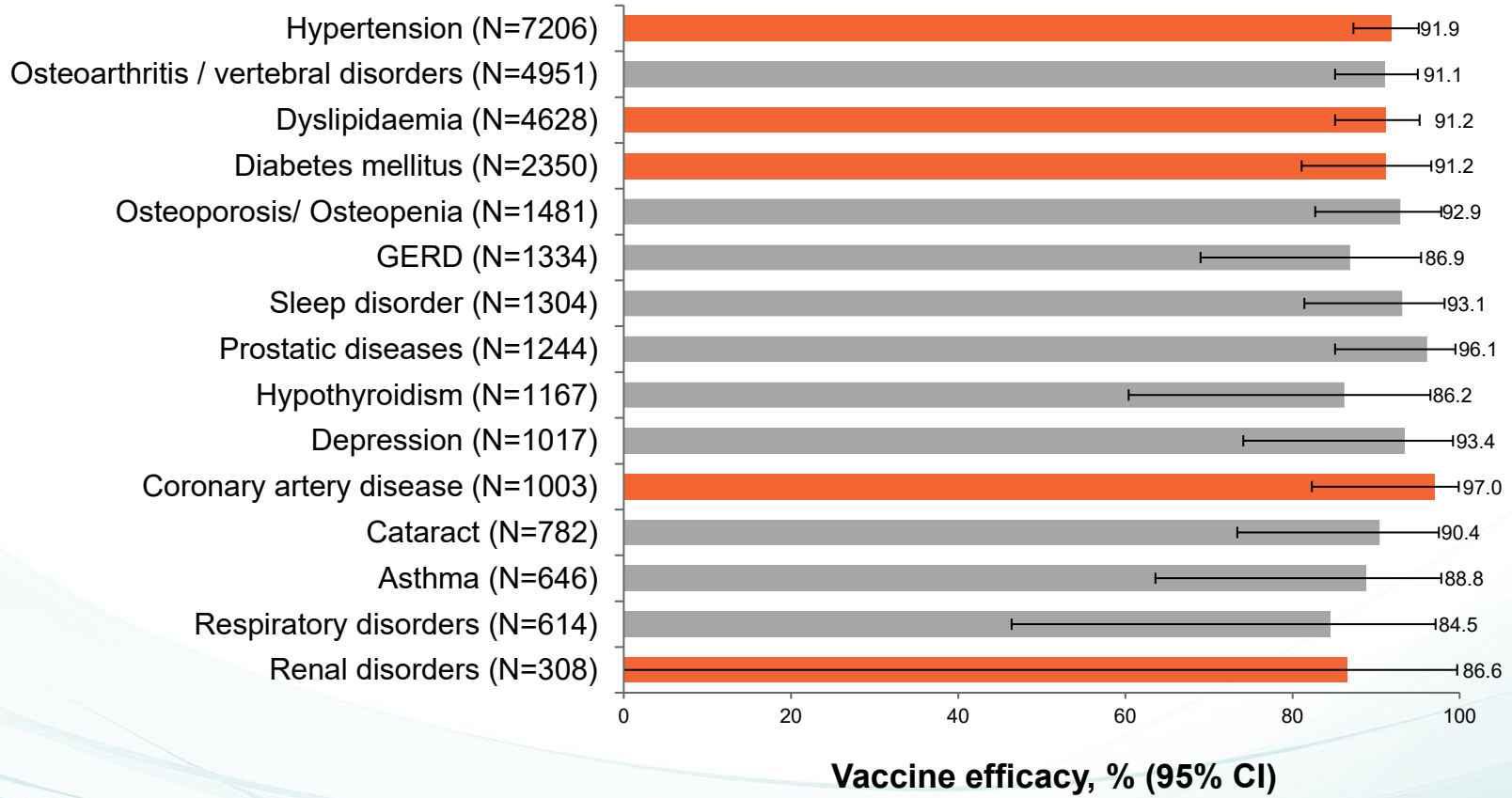


Figure adapted from GSK RSVPreF3 Vaccine for Respiratory Syncytial Virus (RSV) in Older Adults Presented at Vaccines and Related Biological Products Advisory Committee March 1, 2023. https://www.fda.gov/media/165649/download (accessed June 2023). *LRTD defined as ≥2 lower respiratory symptoms/signs for ≥24 hours including ≥1 lower respiratory sign, or ≥3 lower respiratory symptoms for ≥24 hours. All RSV cases confirmed by RT-PCR; †COPD, asthma, any chronic respiratory/pulmonary disease, diabetes type 1 or type 2, chronic heart failure, advanced liver or renal disease. COPD, chronic obstructive pulmonary disease; CI, confidence interval; LRTD, lower respiratory tract disease; RT-PCR, reverse-transcriptase polymerase chain reaction 1. GSK RSVPreF3 Vaccine for Respiratory Syncytial Virus (RSV) in Older Adults Presented at Vaccines and Related Biological Products Advisory Committee March 1, 2023. https://www.fda.gov/media/165649/download (accessed June 2023); 2. Papi A *et al. N Engl J Med* 2023;388(7):595–608

RZV Vaccination Against HZV by Comorbidity

Pooled post-hoc analysis RZV trials show efficacy in older adults with various comorbidities

Vaccine efficacy against HZV for participants with medical conditions at enrolment,* over ~4 years' follow-up

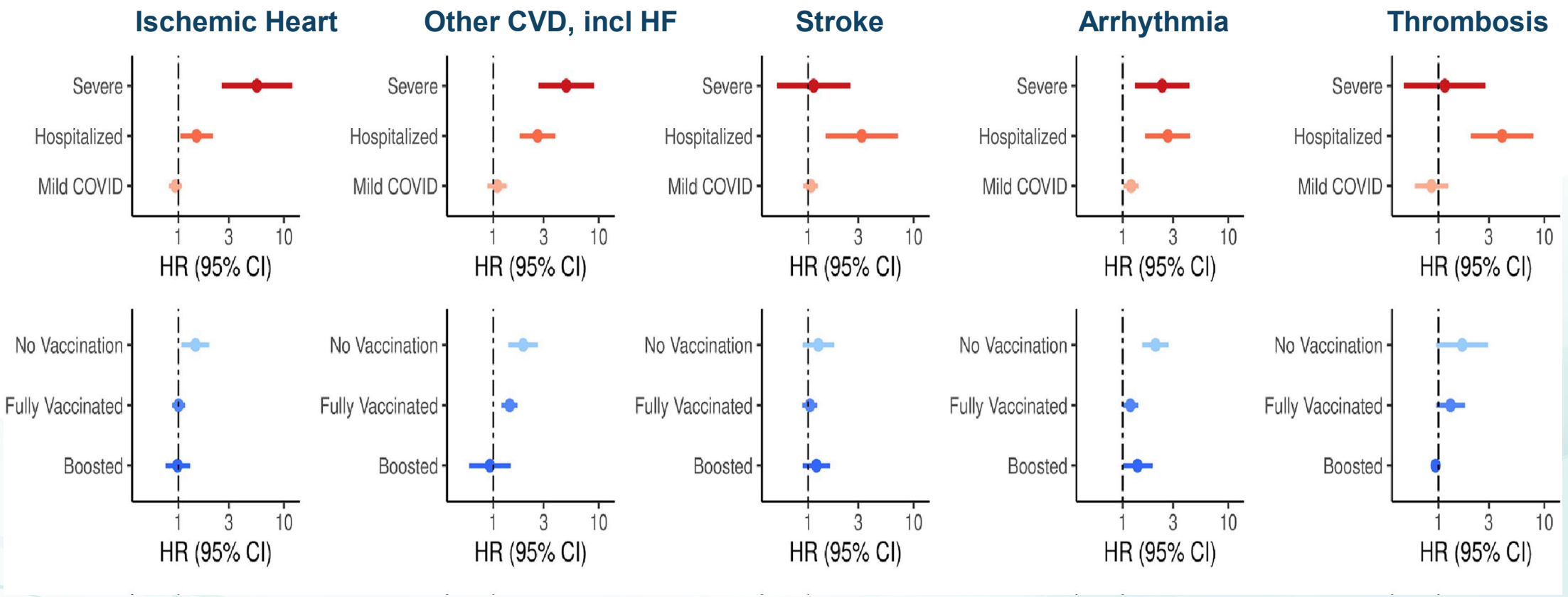


The numbers of SAEs, deaths and pIMDs were similar in the vaccine and placebo groups for each of the medical conditions

No safety concerns were identified based on baseline medical condition

Post-hoc subgroup analyses of safety and efficacy by participants' pre-existing conditions were exploratory. *No standard definitions were used in the diagnosis; therefore, each selected medical condition could vary with respect to severity, stage, treatment, progression or type (eg DM type). CI, confidence interval; DM, diabetes mellitus; GERD, gastro-oesophageal reflux disease; HZ, herpes zoster; pIMD, potential immune-mediated disease; RZV, recombinant zoster vaccine; SAE, serious adverse event. Oostvogels L et al. *Hum Vaccin Immunother* 2019;15:2865–2872. Lal H et al. *NEJM* 2015;372:2087–2096; 2. Cunningham AL et al. *NEJM* 2016;75:1019–1032.

Risk of Cardiovascular, Stroke, and Thrombotic Events by Severity of COVID-19 Infection + Vaccination Status



* Using national healthcare databases from Singapore

1. Lim JT et al. *Clin Infect Dis* 2024;78:70-79.

Canadian Recommendations: Influenza Vaccination

Recipient by age group	Vaccine types authorized for use	Recommendations
18-59 yrs	• IIV4-SD • IIV4-cc • RIV4 • LAIV4	• Any available vaccines should be used if no contraindications/precautions • LAIV not recommended if pregnant or with chronic health condition identified in List 1, incl. immune compromising conditions, and health care worker - Use IIV or RIV instead
60-64 yrs	• IIV4-SD • IIV4-cc • RIV4	• Any available vaccines should be used if no contraindications
65 yrs +	• IIV3-Adj • IIV4-SD • IIV4-HD • IIV4-cc • RIV4	• Any available vaccines should be used if no contraindications

Abbreviations:

ART: antiretroviral therapy
HAART: highly active antiretroviral therapy
IIV: inactivated influenza vaccine
IIV3-Adj: adjuvanted trivalent inactivated influenza vaccine
IIV4-cc: quadrivalent mammalian cell culture-based inactivated influenza vaccine
IIV4-HD: high-dose quadrivalent inactivated influenza vaccine
IIV4-SD: standard-dose quadrivalent inactivated influenza vaccine
RIV4: quadrivalent recombinant influenza vaccine
LAIV4: quadrivalent live attenuated influenza vaccine

https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-10-influenza-vaccine.html

Canadian Recommendations: RSV Vaccination

- Authorized for use in Canada in adults 60+
- Awaiting NACI recommendations
- CDC Advisory Committee on Immunization Practices (ACIP):
  - Adults aged ≥60 years may receive a single dose of RSV vaccine, using shared clinical decision-making:
    - Consider patient's risk for severe RSV-associated disease
    - Epidemiologic evidence: persons ≥60 years who are at highest risk for severe RSV disease and might be most likely to benefit from vaccination include those with:
      - chronic medical conditions (lung diseases, incl. COPD and asthma)
      - **cardiovascular diseases (CHF, CAD)**
      - moderate or severe immune compromise (attributable to a medical condition or receipt of immunosuppressive medications/treatment)
      - diabetes mellitus

Melger *et al.*, 2023. *MMWR* 72: 793

Canadian Recommendation: Herpes Zoster Vaccination

☑ The recombinant zoster vaccine (RZV) is only vaccine authorized for use in Canada

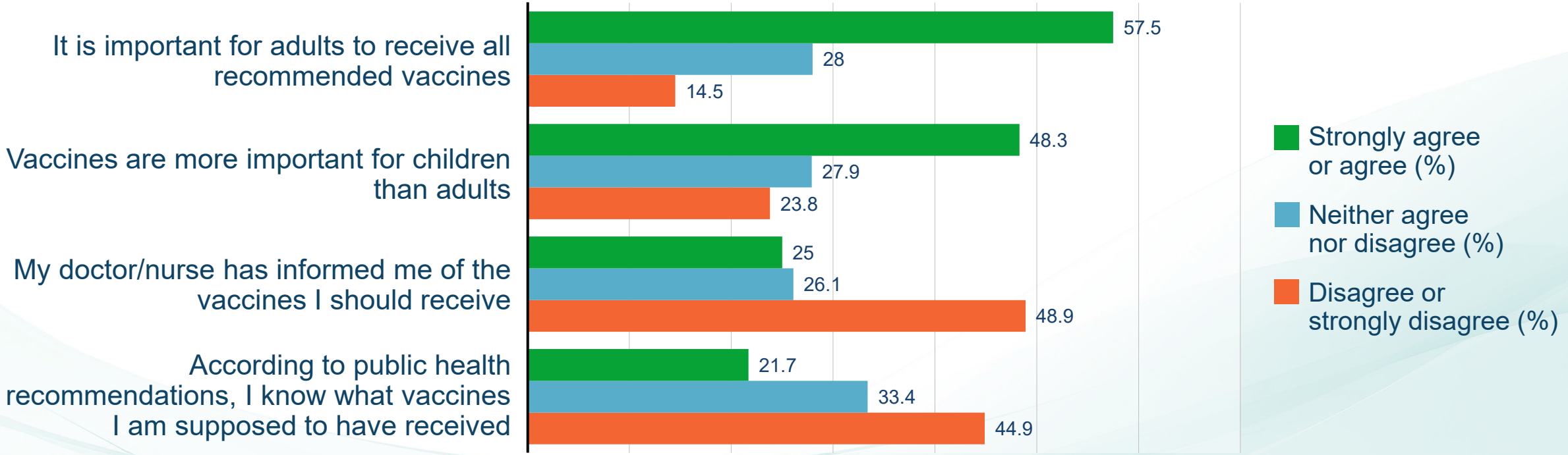
☒ Live-attenuated zoster vaccine (LZV) first authorized in 2008 was discontinued in 2023

- RZV is recommended for individuals ≥50 years of age
  - without contraindications
  - who received LZV, or who have had a previous episode of HZ, should be vaccinated with RZV after at least one year
- RZV indicated for adults 18+ years who are or will be at increased risk of HZ due to immunodeficiency or immunosuppression caused by known disease or therapy

https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-8-herpes-zoster-(shingles)-vaccine.html

However, Only 1 in 5 Canadian Adults are Aware of Which Vaccinations They Should Receive

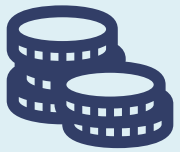
And approximately half have not been informed of which vaccines they need by physician/nurse



Study of 4,023 adults who completed a survey, 62 participated in focus groups; 1,167 healthcare providers (doctors, nurses, pharmacists) completed survey, 45 participated in focus groups. MacDougall DM, et al. *BMJ Open* 2015; 5:e009062.

Perceived Barriers to Immunization Differ Between Patients and Physicians

#1 Barrier to Vaccine Uptake Among Canadian Physicians[1]



Perceived Barriers of Cost

- **Cost** was seen as the number one barrier by **92% to 95%** of physicians
- Perceived barriers may **limit recommendations for vaccination**, particularly among older women or men

#1 Barrier to getting Vaccinated Among Canadian Adults[2]

Receiving an HCP Recommendation

- The number one reported barrier to vaccination for the general public was **not having a recommendation from an HCP**
- **Cost** was seen as a barrier by **only 18% (male)** and **19% (female) of participants**

- It is important to counsel patients on all available vaccines, without making any presumptions as to what they can or cannot afford

1. Steben et al. *J Obstet Gynaecol Can*. 2019;41:599-607; 2. Steben et al. *J Obstet Gynaecol Can*. 2019;41:1125-33.

Practice Points for Optimizing Immunization Rates in CV Patients

1 DISCUSS
Make it routine

Build a habit of talking about vaccination

Prioritize prevention
Ensure immunization discussions aren't lost amid other concerns

Take responsibility for the discussion
Don't assume another HCP will take the lead

2 RECOMMEND
Make it clear

Make the recommendation
Recommendations to vaccinate are a major factor in ensuring patient and primary care provider reassurance

Help your patient understand why
Ensure your patients understand their risk factors for potential complications of viral diseases and the importance of prevention

Take a presumptive approach
Telling rather than asking about vaccinations is seen as a stronger recommendation

3 ADMINISTER
Make it easy

Engage your allied health team to discuss, recommend, and administer vaccinations

Ensure patients know where they can go to receive their vaccines

Patient materials
Take advantage of or develop vaccination information to aid in counselling your patients

Add vaccination prompts to EMR and include vaccination recommendations in discharge plans

EMR, electronic medical record; HCP, health care provider.

Q & A Period

Dr. Jacob Udell & Dr. Shelley Zieroth

THANK YOU!

Please remember to complete the session evaluation

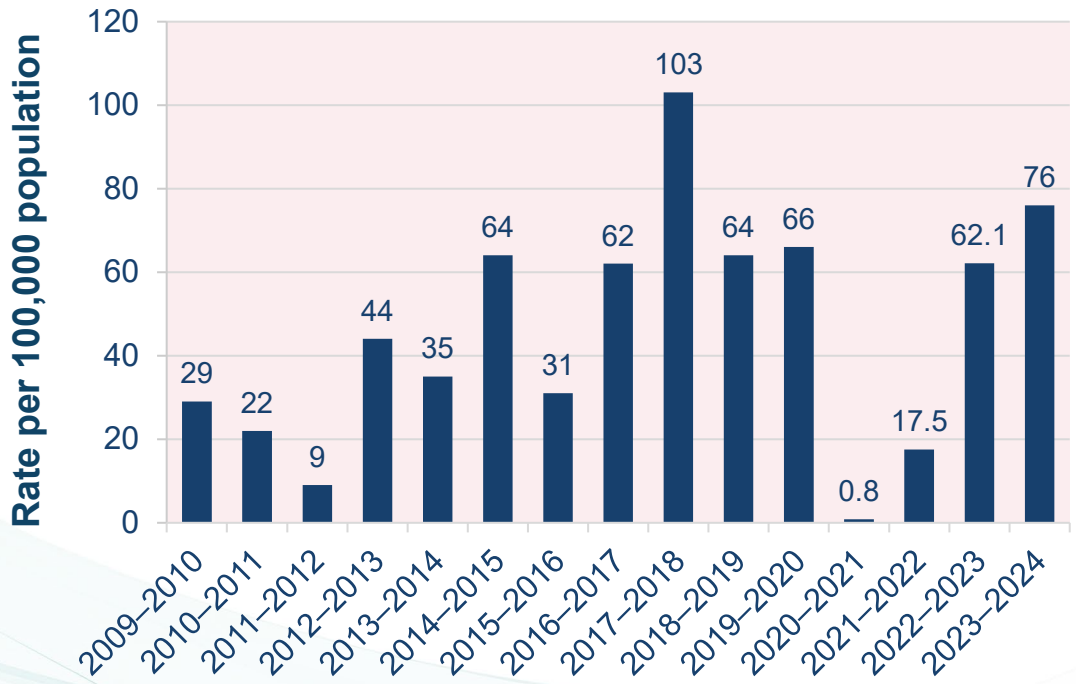
Next up! Please proceed to the 36th floor for the workshops

This program has received an educational grant from GSK Canada. This program was developed by the Canadian Heart Failure Society and was planned to achieve scientific integrity, objectivity and balance.

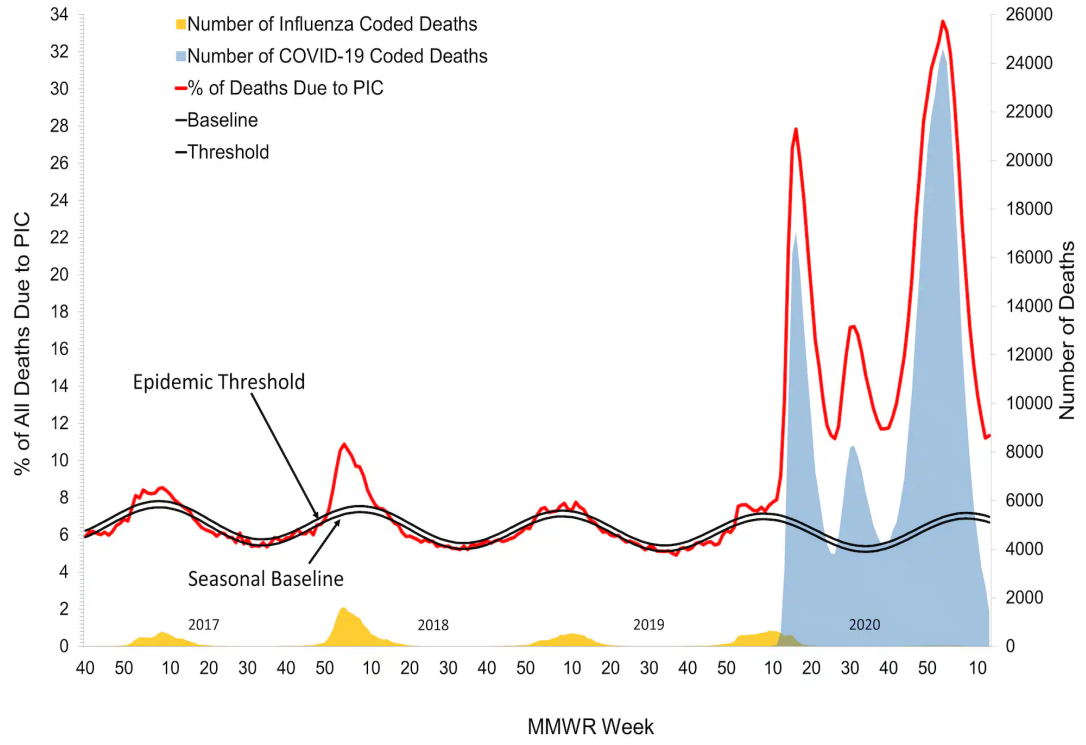
Typical Influenza Season Illness vs COVID-19

360K hospitalized, 21K deaths in the USA in 2022/23[1]

Cumulative influenza hospitalization rates[2]



% of deaths from pneumonia, influenza, COVID-19 by week[3]



ILI, influenza-like illness; MMWR, Morbidity and Mortality Weekly Report; PIC, pneumonia, influenza, COVID-19

1. CDC, 2024. https://www.cdc.gov/flu/about/burden; 2. CDC, 2024. https://gis.cdc.gov/GRASP/Fluview/FluHospRates.html; 3. CDC, 2021. https://www.cdc.gov/flu/weekly/weeklyarchives2020-2021 (URLs accessed April 2024).

COVID-19 Vaccine and Risk of Myopericarditis

Table 2a
Myocarditis and/or pericarditis rates in males by age group, dose number, and mRNA vaccine product.

Age (yrs)	V								Attributable Fraction
18–29	n							2)	86.53%
18–29	B							2)	73.12%
18–29	n							81)	97.80%
18–29	B							)	88.62%
30–39	n							)	29.33%
30–39	B							5)	46.00%
30–39	n							)	90.59%
30–39	B							4)	64.54%

Table 2b
Myocarditis and/

Age (yrs)	V								isk	Attributable Fraction
18–29	r								.50)	81.75%
18–29	F								.64)	70.88%
18–29	r								3)	95.50%
18–29	F								8)	84.62%
30–39	r								2)	75.00%
30–39	F								.78)	74.22%
30–39	r								3)	94.25%
30–39	F								8)	83.08%

[1] Per 100,000 doses administered.
[2] Reported number of myocarditis and/or pericarditis in excess of expected background cases.

Table 4
Rate ratio estimates from stratified Poisson models comparing mRNA-1273 versus BNT162b2 risk for myocarditis and/or pericarditis after dose 2, conditioned on week vaccine was administered, stratified by age and sex.

	N (reports of myocarditis and/or pericarditis)	RR (95% CI)(mRNA-1273 vs BNT162b2)	P-value
Males 18–29*	186	4.72 (3.09 – 7.39)	<0.001
Males 30–39*	40	3.52 (1.61 – 8.29)	0.01
Females 18–29	31	2.67 (1.28 – 5.78)	0.01
Females 30–39	25	3.99 (1.76 – 9.60)	0.001

* Models were over dispersed so quasi-Poisson models were used to adjust the standard errors (Deviance/degrees of freedom greater than 1.5)

Abraham N, *et al*. Vaccine. 2022;40:4663-4671.

COVID-19 Vaccine Booster Recommendations

- For those previously vaccinated against COVID-19, NACI recommends a dose of the XBB.1.5-containing formulation of COVID-19 vaccine…if at least 6 months from previous COVID-19 vaccine dose or known SARS-CoV-2 infection (whichever is later).
- Immunization is particularly important for those at increased risk of COVID-19 infection or severe disease, e.g.:
  - Adults 65 years +
  - Residents of long-term care homes/other congregate living settings
  - Underlying medical conditions that place people at higher risk of severe COVID-19
  - Pregnant women
  - First Nations, Métis and Inuit communities
  - Members of racialized and other equity-deserving communities
  - People who provide essential community services
  - (Strong NACI Recommendation)

https://www.canada.ca/en/public-health/services/publications/vaccines-immunization/national-advisory-committee-immunization-addendum-guidance-use-covid-19-vaccines-fall-2023.html

COVID-19 Vaccine Recommendations (primary series): Myocarditis/pericarditis (mRNA Vaccines)

*"…primary series surveillance data in Canada, US and European Nordic countries suggest a **higher rate of myocarditis/pericarditis cases reported after vaccination with Moderna Spikevax original (100 mcg) compared to Pfizer-BioNTech Comirnaty original (30 mcg) vaccine,** especially among 12- to 29-year-old males following a 2nd dose of vaccine."*

- Evidence from bivalent and original mRNA COVID-19 vaccines across different age groups shows:
  - the **risk of myocarditis is lower following boosters compared to dose 2 of the primary series**
  - **no product-specific identifiable difference in the risk of myocarditis** following a booster dose
  - these observations were also seen in adolescents 12-17 years of age, however the use of Moderna Spikevax COVID-19 vaccines have been limited in those 5-17 years

As a result of this safety signal, Pfizer-BioNTech Comirnaty was preferentially recommended as a primary series for those between 12-29 years of age

https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-26-covid-19-vaccine.html#a5.2